

## REMARKS

Applicants respectfully thank the Examiner for finding the previous amendment persuasive and withdrawing the previous rejections.

### The Present Invention

The present invention addresses the problem of providing an alternative treatment for the signs of aging by employing a unique combination of retinoid, retinoid booster, and phytoestrogen. However, it has been discovered that *boosters* and *phytoestrogens*, while boosting the benefits of retinoids, destabilize the retinoid by inducing oxidation of retinol. For example, glycerrhetic acid contributes to 1.6-Fold increase in the rate of retinol loss (see Table 1, Specification at page 40). The present invention addresses the problem of providing a stable skin care product with maximum efficacy, by preventing any undesired interaction of the retinoid and the boosting agents and the phytoestrogens during storage. Therefore, the present invention provides the phytoestrogen as part of the second composition in the second compartment of the dual compartment package, to further enhance (synergistically) the effect of the first benefit.

**The Present Invention is Not Obvious under 35 USC § 103**

**Granger et al. and Pillai et al. in view of Liu et al. and Suares et al.**

Claims 1-2 , 5-6 and 9 were rejected under 35 USC § 103 as being unpatentable over Granger et al., U.S. 5,723,139 and Pillai et al. US 6,548,072 in view of Liu et al., US. 5,976,555 and Suares et al. , U.S. 5,941,116. Applicants respectfully traverse.

Firstly, there is no suggestion or motivation to combine the references and, secondly, Applicants have shown unexpected results in the combination of ingredients, i.e. synergistic results from combination of retinoid and boosters and phytoestrogen. The particular means by which the compositions are separated is new and inventive, and critically contributes to the stability of retinoids without compromising overall efficacy.

As suggested in the Office Action that Granger et al. '139, while disclosing retinoid and booster, do not teach or suggest the claimed phyto-estrogens. Also, Granger et al. '139 do not teach or suggest the storage of a first composition comprising retinoid, and second composition comprising retinoid booster, phyto-estrogens, in separate compartments joined together.

Pillai et al. '072 is cited for its disclosure of phytoestrogens, however, Applicants have shown strong evidence of unexpected, synergistic results, as discussed below. The Examiner appears not to have considered or commented on the evidence of unexpected results presented in the Specification and the Declaration. Claim 9 is specifically directed to the showing in the Declaration.

Liu et al disclose a container for use for the retinoid composition with an emulsifier system and a co-emulsifier alone and does not protect the retinoid from degradation due to contact with retinoid boosters and with phytoestrogens. Liu et al. do not address the problem to which the present invention is addressed, i.e., alleviating the additional instability contributed by boosters and phytoestrogens. The combination of specified retinoids with specified boosters of claim 1 are not taught or suggested by Liu et al. The combination of at least 2 boosters as claimed in present claim 2 are not taught or suggested by Liu et al. either alone or in combination with the primary references.

Suarez et al. (USPN 5,914,116) *teach away from the present invention*. Suares et al. disclose two separate containers for separating two different skin actives **for two different benefits**, with one container containing a first active providing a first benefit and the second containing a second active providing a second and different benefit. See Suares et al at col. 11, lines 13-15 (" ... the first and second actives and benefits being different from one another..."). Furthermore, Suares et al. fail to disclose the need to separate phytoestrogens from retinoids. In contrast, the present invention is directed to two separate compositions with one intended to boost the benefit of the other. According to the present invention, the two compositions are intended to be applied simultaneously or consecutively, but are kept separately for stability reasons. Independent claim 5, as worded to relate to "first benefit", is intended to clearly convey that the specified retinoids and the phytoestrogens, although separated into two compartments, are there for the same benefit (as compared with the cited art). The first composition provides a first benefit to the skin while the second composition works to boost or enhance the effect of the first benefit. As such, Suares et al *teach away from the present invention* and fail to provide a suggestion or motivation for the particular way the compositions of the present invention are stored separately.

*Storage of the compositions in separate containers is novel and unobvious* because None of the cited documents addresses the problem of retinoid stability in the presence of phytoestrogens and/or boosters. Consequently, there is no suggestion for a person skilled in the art to try to physically separate the retinoids, the boosters, and the phytoestrogens. For example, Table 1 at page 40 of the Specification shows that glycerhetic acid contributes to 1.6-fold and linoleic acid contributes to 3.4-fold increase in the rate of retinol loss. Absent the hindsight of Applicants' specification, there would be no suggestion or motivation for one skilled in the art to separate the retinoid and booster compositions.

In particular, none of the cited references teaches or suggests a two-part composition which contains in one part a retinoid, and in the second part a retinoid booster and a phytoestrogen. There is no teaching or suggestion of how to put these components together to achieve a stable skin care product. Suares et al. do not remedy the defect because they fail to teach or suggest which combinations of components are placed together and which are kept separate. Only with the hindsight of the present invention is this combination possible.

**Granger et al., Pillai et al., and Meybeck in view of Liu et al. and Suares et al.**

Claims 1-2, 5-6 and 10 were rejected under 35 USC § 103 as being unpatentable over Granger et al., U.S. 5,723,139, Pillai et al. US 6,548,072, and Meybeck, FR 2 777 179, in view of Liu et al., U.S. 5,976,555 and Suares et al., U.S. 5,941,116. Applicants respectfully traverse.

In addition to the deficiencies discussed above, Granger et al. do not teach or suggest Phophatidylcholine. Granger et al. do not teach or suggest the storage of first composition comprising retinoid, and second composition comprising retinoid boosters, phytoestrogens, in separate compartments joined together.

Meybeck appear to be directed to a cosmetic vehicle containing siloxane. Just because Meybeck appear to disclose phosphatidyl choline and glycyrretic acid somewhere in its disclosure, would not make it obvious for one skilled in the art to combine these materials with retinoids and with retinoid boosters in a dual compartment package to come up with the present invention. The Examiner is picking and choosing elements from numerous references and is not viewing the invention as a whole. Moreover, strong evidence of unexpected, synergistic, results that has been presented must be considered. Liu et al. and Suares et al. have been discussed above, and the combination with Meybeck in addition to previously cited references still either fails to make out a *prima facie* case of obviousness and/or is overcome with evidence of unexpected results. Accordingly, the present application should be allowed to issue without further delay.

Some teaching, suggestion, or incentive supporting combination of multiple references must be shown in order to prove obviousness. In re Gaiger, 815 F.2d 686

(Fed. Cir. 1987); ACS Hospital Systems, Inc. v. Montefiore Hospital, 221 U.S.P.Q. 929, 933 (Fed. Cir. 1984).

An obviousness rejection is proper only when “the subject matter as a whole would have been obvious at the time the invention was made ...” (emphasis added). 35 U.S.C. 103. Applicants respectfully submit that the Office Action has improperly chosen certain aspects of one reference and combined them with aspects of other references, without showing where the motivation is to combine them to come up with the subject matter of the present invention as a whole, within the meaning of 35 U.S.C. 103. Applicants submit that the pending claims are not obvious over the cited references, under 35 U.S.C. 103. Reconsideration and withdrawal of the rejection is respectfully requested.

**Evidence of Unexpected, Synergistic, Results Must Be Considered**

Applicants do not consider that the Examiner has set forth a *prima facie* case of obviousness. Even if such a case had been set forth, applicants have demonstrated unexpected results. Applicants have demonstrated strong *synergies* in the combination of retinoids with phytoestrogens. See Specification, Tables 4 and 5 at pp. 48-49. At the same time, Applicants have demonstrated that phytoestrogens contribute to loss of stability of retinoids and therefore require a dual compartment package. See Specification, Example 5, Tables 6 and 7. These are *clear and convincing*, unexpected results, rebutting any *prima facie* case of obviousness if it had been made out.

Furthermore, Applicants have submitting a Rule 132 Declaration in support of strong synergies of retinoids with B2 and B3 boosters. In particular, the data show a more than additive effect of Glycyrrhetic acid and Phosphatidyl choline (B2) in boosting retinol activity to inhibit transglutaminase production. Specifically, the combination of phosphatidyl choline and glycyrrhetic acid resulted in about 27 % inhibition, while each individually resulted in about 2 % and about 8 %, respectively. The Declaration supports unexpected results as claimed; particularly, in claims 2, 6, 9 and 10.

**CONCLUSION**

The Office Action has combined **Granger et al., U.S. 5,723,139** and **Pillai et al. US 6,548,072** in view of **Liu et al., US. 5,976,555** and **Suarez et al.** and has

concluded that the claimed invention is obvious. Even if it was not clear prior to the present Amendment, it is now clear that there is no motivation to combine the references. Some teaching, suggestion, or incentive supporting combination of multiple references must be shown in order to prove obviousness. In re Gaiger, 815 F.2d 686 (Fed. Cir. 1987); ACS Hospital Systems, Inc. v. Montefiore Hospital, 221 U.S.P.Q. 929, 933 (Fed. Cir. 1984). For example, there is no suggestion in Liu et al. that actives are unstable as a result of contact with each other, and therefore motivation to combine references with it is lacking.

An obviousness rejection is proper only when “the subject matter as a whole would have been obvious at the time the invention was made ...” (emphasis added). 35 U.S.C. 103. Applicants respectfully submit that the Office Action has improperly chosen certain aspects of one reference and combined them with aspects of other references, without showing where the motivation is to combine them to come up with the subject matter of the present invention as a whole, within the meaning of 35 U.S.C. 103. Applicants submit that the pending claims are not obvious over the cited references, under 35 U.S.C. 103, especially in view of the present Amendment. Reconsideration and withdrawal of the rejection is respectfully requested.

Reconsideration of the rejection is respectfully requested in view of the above claim amendments and remarks. It is respectfully requested that the application be allowed to issue.

Respectfully submitted,

  
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